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That 'Academic' Work on DNA Applied to a Human Disease

EXCITEMENT about the new biology of DNA has tended to provoke either of two reactions: that little men would soon be synthesized and come swarming out of the laboratories or that the whole study of molecular biology was mainly of academic importance and we would see little practical impact of it within our lifetime.

More sensible observers have suggested that we would see ever deeper insight into cancer and other cell pathology over the coming years and decades. It is gratifying, and a little surprising, to see how quickly a concrete application of DNA enzymology has arisen in relation to a human disease.

DNA, or deoxyribonucleic acid, is the substance within the cells that controls heredity.

XERODERMA PIGMENTOSUM is a rare disease which once occupied a prominent place in the textbooks mainly because its gene was wrongly located on the sex chromosome. In fact, it now seems that the Xeroderma gene is located on the same chromosome as the ABO blood group factors. In addition, most of the diagnosed cases belong to the O blood group, which

speaks for some developmental association of the disease with the O group factors.

The principal manifestation of Xeroderma is the sensitivity of the skin to sunlight, specifically to ultraviolet light. Besides excessive "sunburn damage," the patients also have a very high liability to cancers of the skin and to malignant melanoma.

Cases in which 20 tumors have been removed are not unusual and most die from their cancers at an early age. The main interest of the disease to medical science, in view of its rarity, is the light it can throw on the biology of cancer, and on freckles, and possibly on relationships between them.

Dr. J. E. Cleaver of the Radiobiology Laboratory, University of California Medical Center, San Francisco, reported remarkable findings on cultured skin cells from Xeroderma patients in the May 18 issue of *Nature* magazine. The DNA of cell nuclei is vulnerable to chemical damage by ultraviolet light, which introduces "thymine dimers" into the normal DNA structure. These abnormal linkages interfere with the fundamental genetic functions of the

DNA molecule and, unless repaired, either kill the cell or introduce mutations into the next generation of DNA.

MOST ORGANISMS, as an adaptation to living on a sun-baked earth, have developed protective pigments to shade their DNA and have also evolved biochemical repair mechanisms to eliminate thymine dimers when they occur. The repair generally involves three steps, each requiring a different enzyme: (1) the recognition and excision of thymine-dimer segments from the DNA; (2) synthesis of patching copies (repair replication) from the alternative strand of the DNA, and (3) healing in the patched segment.

The biochemical research on DNA repair is closely related to the recent success in replicating a bacterial virus. Nothing could be more academic, nor seemingly more distant from human affairs, than the genetic studies of sex in bacteria that also underlie much of this kind of work, and which have made sporadic entertainment for Congressmen poking fun at research.

Dr. Cleaver reported that Xeroderma cells are defective in the process of DNA

repair after ultraviolet damage. Further work is in progress to determine which of the essential enzymes is altered in the cells from the Xeroderma patients. The process of DNA repair is obviously an essential part of our inherent biological resistance to cancer, with which we dispense only at our peril.

This work exemplifies the excellent biomedical research at our universities, supported by agencies like the Atomic Energy Commission, the National Institutes of Health and the National Science Foundation. Its further growth, however, is being strangled in the budgetary crunch between the President and Congress. It is no consolation that their children will share in paying the price of their neglect.

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